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Design of Chiral Ligands for Asymmetric Catalysis

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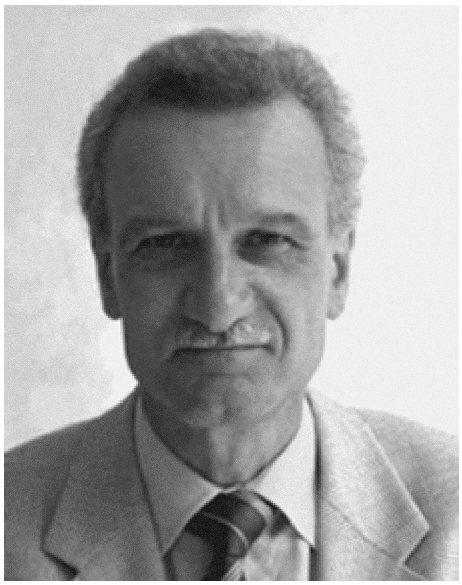

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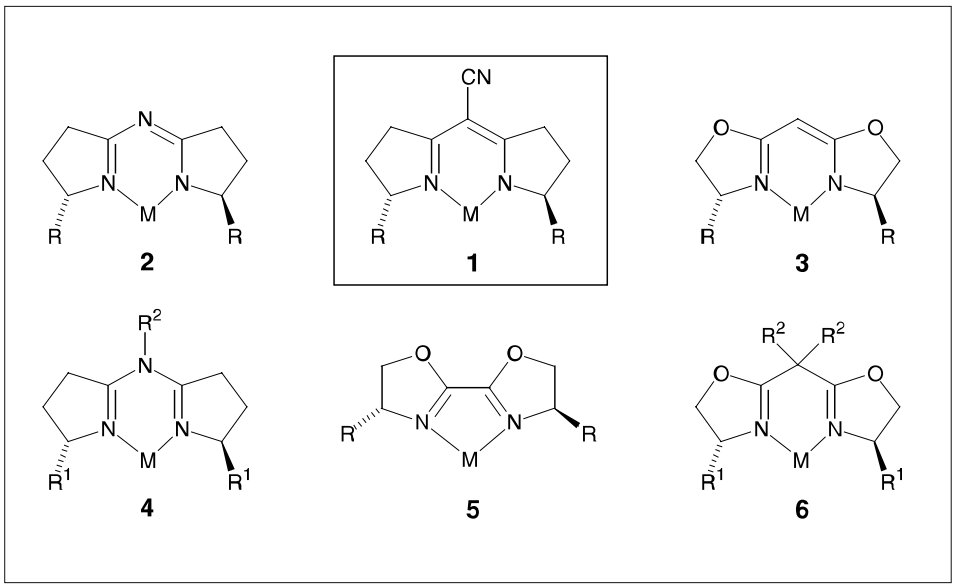

Fig. 1.

In the mid 80s we developed a new class of chiral bidentate nitrogen ligands for asymmetric catalysis, the C_2-symmetric semicorrins **1** (Fig. 1) [1]. In these compounds, the two substituents at the stereogenic centers are located in close proximity to the metal center and, therefore, have a distinct, direct effect on a reaction taking place in the coordination sphere. The high enantioselectivities induced by semicorrins in the copper-catalyzed cyclopropanation of olefins and cobalt-catalyzed conjugate reduction of α,β-unsaturated carboxylic acid derivatives, prompted us and a number of other groups to develop structurally related ligands such as the aza-semicorrins **2** and **4** and the bisoxazolines **3**, **5**, and **6**. Especially bisoxazolines of type **6** have proven to be highly versatile ligands for the enantiocontrol of a wide range of metal-catalyzed processes [1][2].

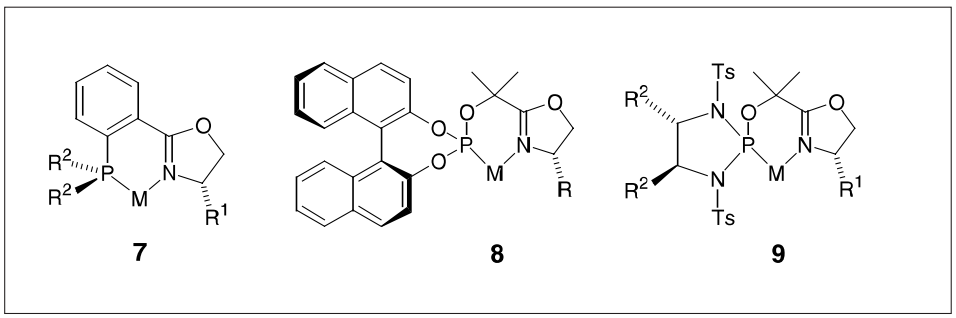

Fig. 2.

In the course of our studies on Pd-catalyzed allylic substitution, we changed the direction of our research toward unsymmetrical P,N-ligands such as **7** (Fig. 2). We hoped that the different electronic *trans* influence of the P- and the N-atom in these ligands could be exploited for controlling the stereochemical course of allylic alkylations, which indeed proved to be the case [3–6]. The modular construction of phosphinooxazoline (PHOX) ligands made it possible to optimize their structure for a particular substrate or reaction. With ligands of type **8** and **9**, which were developed based on mechanistic criteria, high regio- and enantioselectivities could be induced in Pd-catalyzed allylic substitutions with monosubstituted allyl substrates [7]. Recently, we also developed an efficient screening method that allowed us to identify suitable ligands for kinetic resolution of allylic esters.

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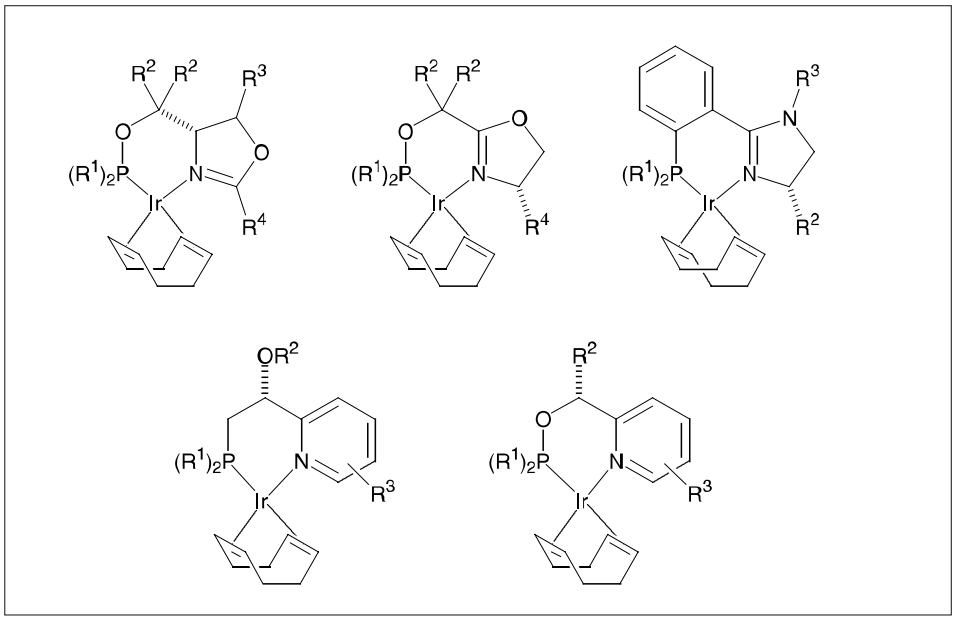

Fig. 3.

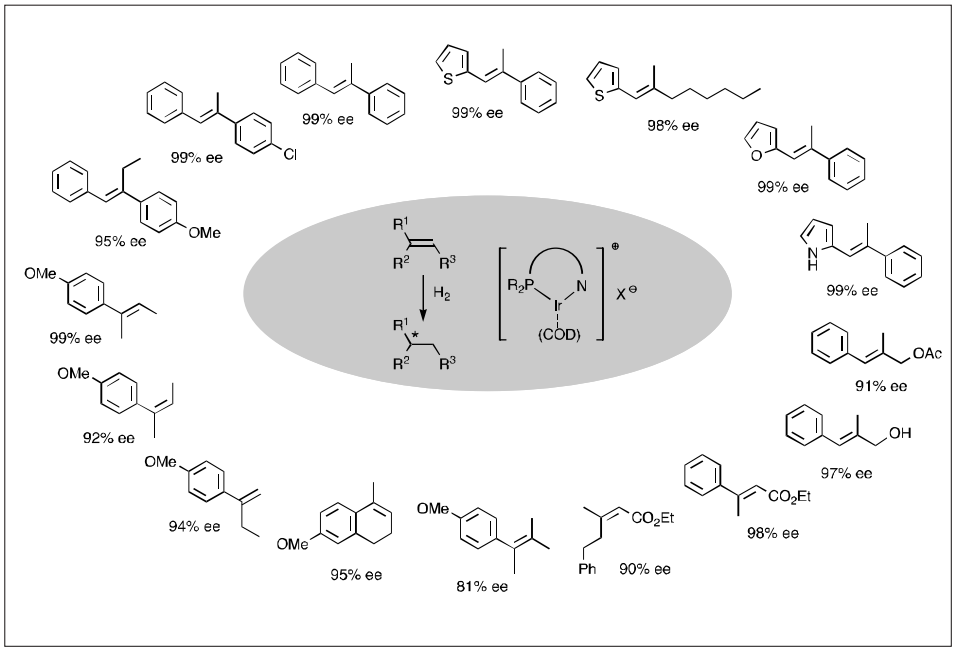

Fig. 4.

PHOX ligands have been successfully applied in various other metal-catalyzed processes, such as Heck reactions, Cu-catalyzed conjugate additions to enones and Ir-catalyzed hydrogenation of imines and olefins [6]. Extensive evaluation of many classes of chiral P,N-ligands has led to a set of Ir complexes that have considerably expanded the scope of asymmetric hydrogenation (Fig. 3) [8]. In contrast to Rh and Ru catalysts, which only perform well with alkenes bearing a polar coordinating group next to the C=C bond, these Ir complexes catalyze the hydrogenation of various unfunctionalized and functionalized, acyclic and cyclic olefins with excellent enantioselectivity and high turn-over numbers (Fig. 4).

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